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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/955,006	09/17/2001	Robert J. Schneider	5914-084-999	7849

20583 7590 04/21/2003

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	12

DATE MAILED: 04/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/955,006	SCHNEIDER ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). *11* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 22-30 are pending.

Response to Amendment

This is a response to the amendment, paper No. 10, filed 20/3/03. Claims 22, 26 and 28 have been amended. Claims 22-23 are pending and considered before the examiner.

Please note any ground of rejection(s) that has not been repeated is removed. Text of those sections of Title 35, U.S. Code not including this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 22-30 are still rejected under 35 U.S.C. 112, first paragraph on the same ground as stated in the previous Office Action, because the specification, while being enabling for using an in vitro cell line system to demonstrate that the expression of recombinant hepatitis B virus (HBV) X protein (HBx) in cell line increase the activation of Src family tyrosine kinases, wherein the activation of the kinase, such as Pyk2, can be inhibited by calcium chelator EGTA or calcium channel poison or modulator cyclosporine A (CsA), does not reasonably provide enablement for having an in vivo method for treating patients infected with HBV by using any or all agents, which are able to modulate the cytosolic calcium concentration of a cells in vitro. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to made and use the invention commensurate in scope with these claims.

3. Applicants transverse the rejection and submit that examiner cannot make the enabling rejection unless there is reason to doubt the objective truth of the teachings which must be relied on for enabling support.

4. Applicants' argument has been fully considered; however, it is not found persuasive because Office does not doubt the in vitro results presented in the specification, however, the in

vitro results cannot be extrapolated into an in vivo practice. For example, specification teaches that use of EGTA treatment results in decreased HBV replication, then Applicants concluded that the reduction of the HBV replication is due to the blockage of the cytosolic calcium level since EGTA is a calcium chelator, which lows down the cytosolic calcium concentration. Based on this, Office cannot accept that any or calcium chelator capable of reducing the cytosolic calcium will be able to inhibit HBV replication and applicable for treating the patient infected with HBV because calcium is an important single molecule that maintains a normal cellular function. Nay thing that influence the cellular function may be influence the virus replication that relied on the cellular components and environment. It is apparently; EGTA or other calcium chelator cannot be use for treating patients in the clinic. It is very unpredictable if patients receive the EGTA or similar compound treatment because there would be a lot of detrimental effects caused by no calcium in the body.

5. In addition, the compounds as claimed by Applicants exhibit quit different structural characteristics, and they must decrease the calcium connection or block the calcium channel or signal through very different ways. Although it is hart to rule out the precise mechanism or relationship between the cytosolic calcium concentration and HBV replication, why Applicants de not use art recognized animal model to testify whether the administrating any or all compounds that are able to low down the cytosolic calcium into the HBV infected animals and see the in vivo outcome, at least the compound that has been used in the vitro assay, such as EGTA, cyclosporin, BAPTA and BAPT-AM can be easily tested.

6. Therefore, the rejection is maintained unless Applicants provide more evidence that support the broadly claimed invention read on using any or all compounds that reduce the cytosolic calcium are able to treat HIB infection in patients.

7. No claims are allowed.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 703-305-1695. The examiner can normally be reached on 7:00 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bao Qun Li
April 18, 2003

James C. Housel 4/21/03
JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600